POEMs

Patient-Oriented Evidence That Matters

Bivalent RSV Vaccine Given to Mothers Reduces Total and Severe RSV Infections in Infants

Clinical Question

Does maternal respiratory syncytial virus (RSV) vaccination safely reduce the likelihood of RSV in their newborns?

Bottom Line

A bivalent RSV vaccine given to pregnant women between 24 and 36 weeks' gestation safely reduces the likelihood of severe RSV in their newborns (number needed to treat [NNT] = 81 at six months of age). (Level of Evidence = 1b–)

Synopsis

The Pfizer-sponsored study evaluated a new RSV vaccine (RSVpreF 60 mcg RSV A and 60 mcg RSV B) in pregnant women. The participating women were healthy, and they received the immunization or placebo injection between 24 and 36 weeks' gestation. A total of 7,392 pregnant women were enrolled; 7,148 of them gave birth. At baseline, mean age was 29 years; mean gestational age was 31 weeks; and 20% were Black, 12.5% were Asian, and 29% were Hispanic. Groups were balanced, but it was not reported whether analysis was per protocol or intention to treat. This is important because retention in the trial was only fair, with approximately 80% still enrolled at six months. Because it was an interim analysis, this may improve in the final analysis. At six months after birth, the likelihood of a medically attended, severe RSV-associated lower respiratory tract illness was significantly lower in the vaccine group (0.5% vs. 1.8%; $P < .05$; NNT = 81). The likelihood of any medically attended RSV lower respiratory tract illness was also lower in the vaccine group at six months (1.6% vs. 3.4%; $P < .05$; NNT = 58). Vaccine efficacy was estimated to be 67% for the outcome of RSV hospitalization. Local reactions occurred in 41% of the vaccine group compared with 10% in the placebo group. Muscle pain was more common in the vaccine group (27% vs. 17%). There were no differences in broader maternal or neonatal outcomes, with five infant deaths in the vaccine group and 12 in the placebo group during follow-up.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Uncertain

Setting: Outpatient (any)

Reference: *Kampmann B, Madhi SA, Munjal I, et al.; MATISSE Study Group. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants.* N Engl J Med. *2023;388(16):1451-1464.*

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Early Return to Activity Improves Symptoms in Children With Concussion

Clinical Question

Is prescribing rest an appropriate treatment for children who are recovering from a concussion?

Bottom Line

Children who have experienced a concussion should not be placed on bed rest but may return to their previous activity level as allowed by the development of new and worsening symptoms. (Level of Evidence = 1a–)

Synopsis

The researchers conducted a systematic review of four databases and identified 24 English-language studies (including 10 randomized controlled trials) of children with concussion to determine the effect of activity on symptoms, quality of life, and

return to preinjury activity levels after a concussion. They followed PRISMA guidelines for conducting and reporting the results. The results from randomized trials were combined for meta-analysis. In seven studies with a total of 269 participants, symptom resolution was slightly better in children who returned to normal activity rather than prescribed rest (standardized mean difference = 0.39; 95% CI, 0.15 to 0.63). Quality of life was not affected by rest vs. return to normal activity, and the rate of return to preinjury activity levels could not be assessed. For study outcomes that could be combined, there was no evidence of heterogeneity among the studies. Risk of bias was high in the randomized controlled studies because of the lack of masking of the children to their treatment assignment. Publication bias was not reported.

Study design: Meta-analysis (other)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: *Chauhan R, Cheng A, Tsow R, et al. Activity and recovery among youth with concussion: a meta-analysis.* Pediatrics. *2023;151(5):e2022059592.*

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Active Surveillance Reduces the Need for Surgery, With No Change in Mortality, at the Price of a Small Increase in Metastatic Disease

Clinical Question

What are the benefits and harms of different approaches to the treatment of screen-detected prostate cancer?

Bottom Line

Active surveillance provides a balance of benefits and harms. After 15 years, for every 100 participants, 40 can avoid the need for surgery with no increase in the risk of death, although three to four more develop metastatic disease than in the groups treated initially with surgery or radiation. (Level of Evidence = 1b)

Synopsis

The ProtecT study group conducted a randomized controlled trial in the United Kingdom that, with its initial publication five years ago, provided the best information available on the benefits and harms of surgery, radiation, and active surveillance for men with screen-detected prostate cancer. Of the 2,664 men with localized prostate cancer detected by screening between 1999 and 2009, a remarkable 1,643 agreed to be randomized to prostatectomy, radiotherapy, or active surveillance. With active surveillance, any patient or physician concern or an increase of at least 50% in prostate-specific antigen level prompted a review, further testing as appropriate, and consideration for therapy. The study reported the outcomes for a median of 15 years following enrollment.

The primary and secondary outcomes were reported per 1,000 person-years, which is difficult to interpret clinically. It can be reframed as 100 patients followed for 10 years, or 67 patients followed for 15 years. The primary outcome of prostate cancer–specific mortality was uncommon, with no significant difference among the groups, ranging from 1.5 to 2.2 deaths per 1,000 person-years (or per 100 men followed for 10 years). There was no significant difference in all-cause mortality. Metastatic disease was approximately twice as likely in the active surveillance group, with an excess of 3.5 more diagnoses of metastatic disease per 1,000 person-years. Patients receiving active surveillance were more likely to start androgen-deprivation therapy (9.4 vs. 5.3 to 5.6 per 1,000 person-years) and experience any clinical progression, which included metastasis, progressing to T3 or T4, requiring androgen deprivation, or having anatomic complications due to tumor growth. By 15 years, approximately 40% of men were able to avoid radiotherapy or surgery.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Hamdy FC, Donovan JL, Lane JA, et al.; ProtecT Study Group. Fifteen-year outcomes after monitoring, surgery, or radiotherapy for prostate cancer.* N Engl J Med. *2023;388(17):1547-1558.*

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Cholesterol-Reducer Evolocumab Associated With a Nonsignificant Increase in Cardiovascular Mortality

Clinical Question

In patients at high risk of cardiovascular death, does the addition of evolocumab (Repatha) to statin therapy decrease cardiovascular-related mortality?

Bottom Line

Published data on the effectiveness of evolocumab in preventing cardiovascular-related mortality may not have represented the actual data in the clinical study report. When causes of death were readjudicated by a masked panel, cardiovascular deaths were numerically higher in the evolocumab group, although not to a level that reached statistical significance. (Level of Evidence = 1b–)

Synopsis

The FOURIER trial, a randomized controlled trial, originally reported a small benefit of evolocumab to reduce cardiovascular events when added to statin treatment in patients at high risk of death due to cardiovascular disease. There was no effect of treatment on cardiovascular or all-cause mortality. The report is a reanalysis of the study. Investigators were able to obtain the Clinical Study Report—the full technical description of the study used to support the approval of a medication—from Health Canada. They discovered that cause of death was determined by the local researcher, presumably not masked to treatment. However, the authors of the reanalysis developed a committee to read the case records of the 870 deaths that occurred in study participants to confirm or refute the stated cause of death. This masked analysis changed the cause of death in almost one-half (41.4%) of the data; when these results were reanalyzed, cardiac deaths were numerically, but nonsignificantly, higher in the evolocumab group (n = 113) than in the placebo group (n = 88; relative risk = 1.28; 95% CI, 0.97 to 1.69; *P* = .078).

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: *Erviti J, Wright J, Bassett K, et al. Restoring mortality data in the FOURIER cardiovascular outcomes trial of evolocumab in patients with cardiovascular disease: a reanalysis based on regulatory data.* BMJ Open. *2022;12(12):e060172.*

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